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DATE: Friday, October 15, 2004

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☐	L12	1998	29
☐	L11	(fluorescent protein or gfp) same fusion protein same (bind$3 or interact$3) same (fragment or domain)	660
☐	L10	L9 same domain	187
☐	L9	L8 same fragment	228
☐	L8	L7 same fusion protein	1018
☐	L7	L6 same (flourescent protein or gfp)	1212
☐	L6	(fluorescent or gfp) same fusion same (bind$3 or interact$3)	3161
☐	L5	L1 same (fluorescent or gfp)	14
☐	L4	L1 same (fluorescent or gfp)	14
☐	L3	Li same (fluorescent or gfp)	5062
☐	L2	L1 and (fluorescent or gfp)	44
☐	L1	protein fragment complementation assay	51

END OF SEARCH HISTORY

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 NEWS  2           "Ask CAS" for self-help around the clock
 NEWS  3  Jul 12   BEILSTEIN enhanced with new display and select options,
                   resulting in a closer connection to BABS
 NEWS  4  AUG 02   IFIPAT/IFIUDB/IFICDB reloaded with new search and display
                   fields
 NEWS  5  AUG 02   CAplus and CA patent records enhanced with European and Japan
                   Patent Office Classifications
 NEWS  6  AUG 02   The Analysis Edition of STN Express with Discover!
                   (Version 7.01 for Windows) now available
 NEWS  7  AUG 27   BIOCOMMERCE: Changes and enhancements to content coverage
 NEWS  8  AUG 27   BIOTECHABS/BIOTECHDS: Two new display fields added for legal
                   status data from INPADOC
 NEWS  9  SEP 01   INPADOC: New family current-awareness alert (SDI) available
 NEWS 10  SEP 01   New pricing for the Save Answers for SciFinder Wizard within
                   STN Express with Discover!
 NEWS 11  SEP 01   New display format, HITSTR, available in WPIDS/WPINDEX/WPIX
 NEWS 12  SEP 14   STN Patent Forum to be held October 13, 2004, in Iselin, NJ
 NEWS 13  SEP 27   STANDARDS will no longer be available on STN
 NEWS 14  SEP 27   SWETSCAN will no longer be available on STN

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               MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP),
               AND CURRENT DISCOVER FILE IS DATED 11 AUGUST 2004
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FILE 'BIOSIS' ENTERED AT 10:03:06 ON 15 OCT 2004
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=> s protein fragment complementation assay
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L1 43 PROTEIN FRAGMENT COMPLEMENTATION ASSAY

=> s l1 and (fluorescent or gfp)
L2 13 L1 AND (FLUORESCENT OR GFP)

=> duplicate remove l2
DUPLICATE PREFERENCE IS 'MEDLINE, BIOSIS'
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PROCESSING COMPLETED FOR L2
L3 8 DUPLICATE REMOVE L2 (5 DUPLICATES REMOVED)

=> d 1-8 bib ab

L3 ANSWER 1 OF 8 MEDLINE on STN DUPLICATE 1
Full Text
AN 2004077559 MEDLINE
DN PubMed ID: 14660642
TI Identification of an additional interaction domain in transmembrane domains 11 and 12 that supports oligomer formation in the human serotonin transporter.
AU Just Herwig; Sitte Harald H; Schmid Johannes A; Freissmuth Michael; Kudlacek Oliver
CS Institute of Pharmacology, University of Vienna Medical School, Wahringer Strasse 13A, A-1090 Vienna, Austria.
SO Journal of biological chemistry, (2004 Feb 20) 279 (8) 6650-7.
Journal code: 2985121R. ISSN: 0021-9258.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200404
ED Entered STN: 20040218
Last Updated on STN: 20040501
Entered Medline: 20040430
AB Na+/Cl--dependent neurotransmitter transporters form constitutive oligomers. The topological arrangement is not known, but a leucine heptad repeat in transmembrane domain (TM) 2 and a glycophorin-like motif in TM6 have been proposed to stabilize the oligomer. To determine the topology, we generated versions of the human serotonin transporter (hSERT) that carried cyan or yellow **fluorescent** proteins at their amino and/or carboxyl terminus. Appropriate pairs were coexpressed to measure fluorescence resonance energy transfer (FRET). Donor photobleaching FRET microscopy was employed to deduce the following arrangement: within the monomer, the amino and carboxyl termini are in close vicinity. In addition, in the oligomer, the carboxyl termini are closer to each other than the amino termini. Hence, a separate interaction domain (i.e. distinct from TM2 and TM6) must reside in the carboxyl-terminal half of hSERT. This was confirmed by expressing the amino- and carboxyl-terminal halves of hSERT. These were retained intracellularly; they also retained the coexpressed full-length transporter by forming export-deficient oligomers and, when cotransfected in all possible combinations, supported FRET. Hence, both the carboxyl and amino termini contain elements that drive oligomerization. By employing fragments comprising two neighboring TM helices, we unequivocally identified TM11/12 as a new contact site by donor photobleaching FRET and beta-lactamase **protein fragment complementation assay**. TM1/2 was also found to self-associate. Thus, oligomerization of hSERT involves at least two discontinuous interfaces. The currently identified interaction sites drive homophilic interactions. This is consistent with assembly of SERT oligomers in an array-like structure containing multimers of dimers.

L3 ANSWER 2 OF 8 MEDLINE on STN DUPLICATE 2
Full Text
AN 2004048932 MEDLINE
DN PubMed ID: 14749367
TI Regulation of apoptosis by the Ft1 protein, a new modulator of protein kinase B/Akt.
AU Remy Ingrid; Michnick Stephen W
CS Departement de Biochimie, Universite de Montreal, Succursale centre-ville, Montreal, Quebec H3C 3J7, Canada.
SO Molecular and cellular biology, (2004 Feb) 24 (4) 1493-504.
Journal code: 8109087. ISSN: 0270-7306.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200403
ED Entered STN: 20040130
Last Updated on STN: 20040313
Entered Medline: 20040312
AB The serine/threonine kinase protein kinase B (PKB)/Akt plays a central role in many cellular processes, including cell growth, glucose metabolism, and apoptosis. However, the identification and validation of novel regulators or effectors is key to future advances in understanding the multiple functions of PKB. Here we report the identification of a novel PKB binding protein, called Ft1, from a cDNA library screen using a green **fluorescent** protein-based **protein-fragment complementation assay**. We show that the Ft1 protein interacts directly with PKB, enhancing the phosphorylation of both of its regulatory sites by promoting its interaction with the upstream kinase PDK1. Further, the modulation of PKB activity by Ft1 has a strong effect on the apoptosis susceptibility of T lymphocytes treated with glucocorticoids. We demonstrate that this phenomenon occurs via a PDK1/PKB/GSK3/NF-ATc signaling cascade that controls the production of the proapoptotic hormone Fas ligand. The wide distribution of Ft1 in adult tissues suggests that it could be a general regulator of PKB activity in the control of differentiation, proliferation, and apoptosis in many cell types.

L3 ANSWER 3 OF 8 MEDLINE on STN
Full Text
AN 2004170211 MEDLINE
DN PubMed ID: 15064473
TI Mapping biochemical networks with **protein-fragment complementation assays**.
AU Remy Ingrid; Michnick Stephen W
CS Departement de Biochemie, Universite de Montreal, Montreal, Quebec, Canada.
SO Methods in molecular biology (Clifton, N.J.), (2004) 261 411-26. Ref: 26
Journal code: 9214969. ISSN: 1064-3745.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, ACADEMIC)
LA English
FS Priority Journals
EM 200407
ED Entered STN: 20040406
Last Updated on STN: 20040730
Entered Medline: 20040729
AB Cellular biochemical machineries, what we call pathways, consist of

dynamically assembling and disassembling macromolecular complexes. Although our models for the organization of biochemical machines are derived largely from in vitro experiments, do they reflect their organization in intact, living cells? We have developed a general experimental strategy that addresses this question by allowing the quantitative probing of molecular interactions in intact, living cells. The experimental strategy is based on **protein-fragment complementation assays** (PCA), a method whereby protein interactions are coupled to refolding of enzymes from cognate fragments where reconstitution of enzyme activity acts as the detector of a protein interaction. A biochemical machine or pathway is defined by grouping interacting proteins into those that are perturbed in the same way by common factors (hormones, metabolites, enzyme inhibitors, and so on). In this chapter we review some of the essential principles of PCA and provide details and protocols for applications of PCA, particularly in mammalian cells, based on three PCA reporters, dihydrofolate reductase, green **fluorescent** protein, and beta-lactamase.

L3 ANSWER 4 OF 8 MEDLINE on STN DUPLICATE 3
Full Text
AN 2004114432 IN-PROCESS
DN PubMed ID: 15003600
TI A cDNA library functional screening strategy based on **fluorescent** protein complementation assays to identify novel components of signaling pathways.
AU Remy Ingrid; Michnick Stephen W
CS Departement de Biochimie, Universite de Montreal, CP 6128, Succursale centre-ville, Montreal, Que, Canada H3C 3J7.
SO Methods (San Diego, Calif.), (2004 Apr) 32 (4) 381-8.
Journal code: 9426302. ISSN: 1046-2023.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS IN-PROCESS; NONINDEXED; Priority Journals
ED Entered STN: 20040309
Last Updated on STN: 20040407
AB Progress towards a deeper understanding of cellular biochemical networks demands the development of methods to both identify and validate component proteins of these networks. Here, we describe a cDNA library screening strategy that achieves these aims, based on a **protein-fragment complementation assay** (PCA) using green **fluorescent** protein (**GFP**) as a reporter. The strategy combines a simple cell-based cDNA-screening approach (interactions of a "bait" protein of interest with "prey" cDNA products) with specific functional assays that use the same system and provide initial validation of the cDNA products as being biologically relevant. We applied this strategy to identify novel interacting partners of the protein kinase PKB/Akt. This method provides very general means of identifying and validating genes involved in any cellular process and is particularly designed for identifying enzyme substrates or regulatory proteins for which the enzyme specificity can only be defined by their interactions with other proteins in cells in which the proteins are normally expressed.

L3 ANSWER 5 OF 8 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN
Full Text
AN 2004:355285 BIOSIS
DN PREV200400355536
TI Identification of an additional interaction domain in TM11/12 that supports oligomer formation in the human serotonin transporter.
AU Just, Herwig; Sitte, Harald; Kudlacek, Oliver kudalcek; Freissmuth,

Michael
SO Naunyn-Schmiedeberg's Archives of Pharmacology, (March 2004) Vol. 369, No. Suppl. 1, pp. R3. print.
Meeting Info.: 45th Spring Meeting of the Deutsche Gesellschaft fuer Experimentelle und Klinische Pharmakologie und Toxikologie. Mainz, Germany. March 09-11, 2004. Deutsche Gesellschaft fuer Experimentelle und Klinische Pharmakologie und Toxikologie.
ISSN: 0028-1298 (ISSN print).
DT Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LA English
ED Entered STN: 5 Sep 2004
Last Updated on STN: 5 Sep 2004

L3 ANSWER 6 OF 8 MEDLINE on STN
Full Text
AN 2004193699 IN-PROCESS
DN PubMed ID: 15090227
TI Measuring drug action in the cellular context using **protein-fragment complementation assays**.
AU Yu Helen; West Mary; Keon Brigitte H; Bilter Graham K; Owens Stephen; Lamerdin Jane; Westwick John K
CS Odyssey Thera, San Ramon, CA 94583, USA.
SO Assay Drug Dev Technol, (2003 Dec) 1 (6) 811-22.
Journal code: 101151468. ISSN: 1540-658X.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS IN-PROCESS; NONINDEXED; Priority Journals
ED Entered STN: 20040420
Last Updated on STN: 20040505
AB Cellular signal transduction occurs in the context of dynamic multiprotein complexes in highly ramified pathways. These complexes in turn interact with the cytoskeleton, protein scaffolds, membranes, lipid rafts, and specific subcellular organelles, contributing to the exquisitely tight regulation of their localization and activity. However, these realities of drug target biology are not addressed by currently available drug discovery platforms. In this article, we describe the use of **protein-fragment complementation assays** (PCAs) to assess drugs and drug targets in the context of their native environment. The PCA process allows for the detection of protein-protein complexes following the expression of full-length mammalian genes linked in-frame to polypeptide fragments of rationally dissected reporter genes. If cellular activity causes the association of two proteins linked to complementary reporter fragments, the interaction of the proteins of interest enables refolding of the fragments, which can then generate a quantifiable signal. Using a PCA based on a yellow **fluorescent** protein, we demonstrate that functional (p50/p65) complexes of the heterodimeric nuclear factor-kappaB transcription factor, as well as the transcription factor subunit p65 and its modulator IkappaBalpha, can be visualized and monitored in live cells. We observed similar responses of the PCA assays to the activities of the cognate endogenous proteins, including modulation by known agonists and antagonists. A proof-of-concept high throughput screen was carried out using the p50/p65 cell line, and potent inhibitors of this pathway were identified. These assays record the dynamic activity of signaling pathways in living cells and in real time, and validate the utility of PCA as a novel approach to drug discovery.

L3 ANSWER 7 OF 8 MEDLINE on STN DUPLICATE 4
Full Text

AN 2002301536 MEDLINE
DN PubMed ID: 12042868
TI Beta-lactamase **protein fragment complementation assays** as in vivo and in vitro sensors of protein protein interactions.
AU Galarneau Andre; Primeau Martin; Trudeau Louis-Eric; Michnick Stephen W
CS Departement de Biochimie, C.P. 6128, Succursale Centre-Ville, Montreal, QC, H3C 3J7, Canada.
SO Nature biotechnology, (2002 Jun) 20 (6) 619-22.
Journal code: 9604648. ISSN: 1087-0156.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
(VALIDATION STUDIES)
LA English
FS Priority Journals
EM 200301
ED Entered STN: 20020604
Last Updated on STN: 20030204
Entered Medline: 20030103
AB We have previously described a strategy for detecting protein protein interactions based on protein interaction assisted folding of rationally designed fragments of enzymes. We call this strategy the **protein fragment complementation assay** (PCA). Here we describe PCAs based on the enzyme TEM-1 beta-lactamase (EC: 3.5.2.6), which include simple colorimetric in vitro assays using the cephalosporin nitrocefin and assays in intact cells using the **fluorescent** substrate CCF2/AM (ref. 6). Constitutive protein protein interactions of the GCN4 leucine zippers and of apoptotic proteins Bcl2 and Bad, and the homodimerization of Smad3, were tested in an in vitro assay using cell lysates. With the same in vitro assay, we also demonstrate interactions of protein kinase PKB with substrate Bad. The in vitro assay is facile and amenable to high-throughput modes of screening with signal-to-background ratios in the range of 10:1 to 250:1, which is superior to other PCAs developed to date. Furthermore, we show that the in vitro assay can be used for quantitative analysis of a small molecule induced protein interaction, the rapamycin-induced interaction of FKBP and yeast FRB (the FKBP-rapamycin binding domain of TOR (target of rapamycin)). The assay reproduces the known dissociation constant and number of sites for this interaction. The combination of in vitro colorimetric and in vivo fluorescence assays of beta-lactamase in mammalian cells suggests a wide variety of sensitive and high-throughput large-scale applications, including in vitro protein array analysis of protein protein or enzyme protein interactions and in vivo applications such as clonal selection for cells expressing interacting protein partners.

L3 ANSWER 8 OF 8 MEDLINE on STN DUPLICATE 5
Full Text
AN 2001431958 MEDLINE
DN PubMed ID: 11479572
TI Direct visualization of protein interactions in plant cells.
AU Subramaniam R; Desveaux D; Spickler C; Michnick S W; Brisson N
CS Department of Biochemistry, Universite de Montreal, Montreal, Canada H3C 3J7.
SO Nature biotechnology, (2001 Aug) 19 (8) 769-72.
Journal code: 9604648. ISSN: 1087-0156.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200110
ED Entered STN: 20011008

Last Updated on STN: 20011008
Entered Medline: 20011004

AB The protein NPR1/NIM1 is required for the induction of systemic acquired resistance (SAR) in plants and has been shown to interact with members of the TGA/OBF family of basic leucine zipper (bZIP) transcription factors. However, to date, there is no method available to monitor such interactions in plant cells. We report here an in vivo **protein fragment complementation assay** (PCA), based on association of reconstituted murine dihydrofolate reductase (mDHFR) with a **fluorescent** probe to detect protein-protein interaction in planta. We demonstrate that the interaction between Arabidopsis NPR1/NIM1 and the bZIP factor TGA2 is induced by the regulators of SAR, salicylic acid (SA), and its analog 2,6-dichloroisonicotinic acid (INA) with distinct species-specific responses. Furthermore, the induced interaction is localized predominantly in the nucleus. **Protein fragment complementation assays** could be of value to agricultural research by providing a system for high-throughput biochemical pathway mapping and for screening of small molecules that modulate protein interactions.

```
=> s (fluorescent or gfp) and fusion and bind
L4        1409 (FLUORESCENT OR GFP) AND FUSION AND BIND

=> s (fluorescent protein or gfp) and fusion protein and (bind or interaction)
L5        1896 (FLUORESCENT PROTEIN OR GFP) AND FUSION PROTEIN AND (BIND OR
               INTERACTION)

=> s l5 and fragment
L6         148 L5 AND FRAGMENT

=> s l6 and domain
L7          91 L6 AND DOMAIN

=> duplicate remove l7
DUPLICATE PREFERENCE IS 'MEDLINE, BIOSIS'
KEEP DUPLICATES FROM MORE THAN ONE FILE?  Y/(N):n
PROCESSING COMPLETED FOR L7
L8           78 DUPLICATE REMOVE L7 (13 DUPLICATES REMOVED)

=> d 1-10 bib ab

L8   ANSWER 1 OF 78     MEDLINE on STN                    DUPLICATE 1
Full Text
AN   2004263910     MEDLINE
DN   PubMed ID: 15031296
TI   A fluorescence cell biology approach to map the second integrin-binding
     site of talin to a 130-amino acid sequence within the rod domain.
AU   Tremuth Laurent; Kreis Stephanie; Melchior Chantal; Hoebeke Johan; Ronde
     Philippe; Plancon Sebastien; Takeda Kenneth; Kieffer Nelly
CS   Laboratoire de Biologie et Physiologie Integree (CNRS/GDRE-ITI),
     Universite du Luxembourg, 162A, Avenue de la Faiencerie, L-1511,
     Luxembourg, France.
SO   Journal of biological chemistry, (2004 May 21) 279 (21) 22258-66.
     Journal code: 2985121R. ISSN: 0021-9258.
CY   United States
DT   Journal; Article; (JOURNAL ARTICLE)
LA   English
FS   Priority Journals
EM   200406
ED   Entered STN: 20040528
```

Last Updated on STN: 20040701
Entered Medline: 20040630

AB The cytoskeletal protein talin, which provides a direct link between integrins and actin filaments, has been shown to contain two distinct binding sites for integrin beta subunits. Here, we report the precise delimitation and a first functional analysis of the talin rod **domain** integrin-binding site. Partially overlapping cDNAs covering the entire human talin gene were transiently expressed as DsRed **fusion proteins** in Chinese hamster ovary cells expressing alpha(IIb)beta(3), linked to green **fluorescent protein** (**GFP**). Two-color fluorescence analysis of the transfected cells, spread on fibrinogen, revealed distinct subcellular staining patterns including focal adhesion, actin filament, and granular labeling for different talin **fragments**. The rod **domain fragment** G (residues 1984-2344), devoid of any known actin- or vinculin-binding sites, colocalized with beta(3)-**GFP** in focal adhesions. Direct in vitro **interaction** of **fragment** G with native platelet integrin alpha(IIb)beta(3) or with the recombinant wild type, but not the Y747A mutant beta(3) cytoplasmic tail, linked to glutathione S-transferase, was demonstrated by surface plasmon resonance analysis and pull-down assays, respectively. Here, we demonstrate for the first time the in vivo relevance of this **interaction** by fluorescence resonance energy transfer between beta(3)-**GFP** and DsRed-talin **fragment** G. Further in vitro pull-down studies allowed us to map out the integrin-binding site within **fragment** G to a stretch of 130 residues (**fragment** J, residues 1984-2113) that also localized to focal adhesions. Finally, we show by a cell biology approach that this integrin-binding site within the talin rod **domain** is important for beta(3)-cytoskeletal **interactions** but does not participate in alpha(IIb)beta(3) activation.

L8 ANSWER 2 OF 78 MEDLINE on STN
Full Text
AN 2004141129 MEDLINE
DN PubMed ID: 14718533
TI The role of the carboxyl terminus in ClC chloride channel function.
AU Hebeisen Simon; Biela Alexander; Giese Bernd; Muller-Newen Gerhard; Hidalgo Patricia; Fahlke Christoph
CS Institutes of Physiology, Rheinisch-Westfalische Technische Hochschule Aachen, Pauwelsstrasse 30, 52074 Aachen, Germany.
SO Journal of biological chemistry, (2004 Mar 26) 279 (13) 13140-7.
Journal code: 2985121R. ISSN: 0021-9258.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200405
ED Entered STN: 20040323
Last Updated on STN: 20040510
Entered Medline: 20040507

AB The human muscle chloride channel ClC-1 has a 398-amino acid carboxyl-terminal **domain** that resides in the cytoplasm and contains two CBS (cystathionine-beta-synthase) **domains**. To examine the role of this region, we studied various carboxyl-terminal truncations by heterologous expression in mammalian cells, whole-cell patch clamp recording, and confocal imaging. Channel constructs lacking parts of the distal CBS **domain**, CBS2, did not produce functional channels, whereas deletion of CBS1 was tolerated. ClC channels are dimeric proteins with two ion conduction pathways (protopores). In heterodimeric channels consisting of one wild type subunit and one subunit in which the carboxyl terminus was completely deleted, only the wild type protopore was functional, indicating that the carboxyl terminus supports the function of the

protopore. All carboxyl-terminal-truncated mutant channels fused to yellow **fluorescent protein** were translated and the majority inserted into the plasma membrane as revealed by confocal microscopy. **Fusion proteins** of cyan **fluorescent protein** linked to various **fragments** of the carboxyl terminus formed soluble proteins that could be redistributed to the surface membrane through binding to certain truncated channel subunits. Stable binding only occurs between carboxyl-terminal **fragments** of a single subunit, not between carboxyl termini of different subunits and not between carboxyl-terminal and transmembrane **domains**. However, an **interaction** with transmembrane **domains** can modify the binding properties of particular carboxyl-terminal proteins. Our results demonstrate that the carboxyl terminus of ClC-1 is not necessary for intracellular trafficking but is critical for channel function. Carboxyl termini fold independently and modify individual protopores of the double-barreled channel.

L8 ANSWER 3 OF 78 MEDLINE on STN
Full Text
AN 2004139076 MEDLINE
DN PubMed ID: 14699116
TI Cytoplasmic **domain**-mediated dimerizations of toll-like receptor 4 observed by beta-lactamase enzyme **fragment** complementation.
AU Lee Hyun-Ku; Dunzendorfer Stefan; Tobias Peter S
CS Department of Immunology, The Scripps Research Institute, La Jolla, California 92037, USA.
NC HL23584 (NHLBI)
SO Journal of biological chemistry, (2004 Mar 12) 279 (11) 10564-74. Journal code: 2985121R. ISSN: 0021-9258.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200405
ED Entered STN: 20040323
Last Updated on STN: 20040520
Entered Medline: 20040519
AB Toll-like receptors (TLRs) detect the presence of microbial challenge and initiate innate immune defensive responses. In this work we have explored the mechanism and role of TLR dimerization in signal transduction using the newly developed technique of beta-lactamase protein **fragment** complementation, among others. We observed that TLR4 **interactions** with itself, with MyD88, or with TLR2 were accurately reported by the enzyme complementation technique. That technique, as well as co-immunoprecipitation, transfection-initiated cell activation, and site-directed mutagenesis all suggest an important role for TLR intracellular **domains** in receptor dimerization. These findings broaden our understanding of TLR self-**interactions** as well as heterodimer formation.

L8 ANSWER 4 OF 78 MEDLINE on STN
Full Text
AN 2004107428 MEDLINE
DN PubMed ID: 14665628
TI Definition of the consensus motif recognized by gamma-adaptin ear **domains**.
AU Mattera Rafael; Ritter Brigitte; Sidhu Sachdev S; McPherson Peter S; Bonifacino Juan S
CS Cell Biology and Metabolism Branch, NICHD, National Institutes of Health, Bethesda, Maryland 20892, USA.
SO Journal of biological chemistry, (2004 Feb 27) 279 (9) 8018-28.

Journal code: 2985121R. ISSN: 0021-9258.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
OS GENBANK-AY367088
EM 200405
ED Entered STN: 20040305
Last Updated on STN: 20040505
Entered Medline: 20040503
AB The heterotetrameric adaptor complex 1 (AP-1) and the monomeric Golgi-localized, gamma ear-containing, Arf-binding (GGA) proteins are components of clathrin coats associated with the trans-Golgi network and endosomes. The carboxyl-terminal ear **domains** (or gamma-adaptin ear (GAE) **domains**) of two gamma-adaptin subunit isoforms of AP-1 and of the GGAs are structurally similar and **bind** to a common set of accessory proteins. In this study, we have systematically defined a core tetrapeptide motif PsiG(P/D/E)(Psi/L/M) (where Psi is an aromatic residue), which is responsible for the **interactions** of accessory proteins with GAE **domains**. The definition of this motif has allowed us to identify novel GAE-binding partners named NECAP and aftiphilin, which also contain clathrin-binding motifs. These findings shed light on the mechanism of accessory protein recruitment to trans-Golgi network and endosomal clathrin coats.

L8 ANSWER 5 OF 78 MEDLINE on STN DUPLICATE 2
Full Text
AN 2004241726 MEDLINE
DN PubMed ID: 15141306
TI Characterization of the yeast tricalbins: membrane-bound multi-C2-**domain** proteins that form complexes involved in membrane trafficking.
AU Creutz C E; Snyder S L; Schulz T A
CS Department of Pharmacology, University of Virginia, Charlottesville, Virginia 22908, USA.. creutz@virginia.edu
NC GM53266 (NIGMS)
SO Cellular and molecular life sciences : CMLS, (2004 May) 61 (10) 1208-20.
Journal code: 9705402. ISSN: 1420-682X.
CY Switzerland
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200407
ED Entered STN: 20040514
Last Updated on STN: 20040710
Entered Medline: 20040709
AB In a survey of yeast genomic sequences encoding calcium- and phospholipid-binding C2 **domains**, three homologous genes were identified that encode proteins that each have three C2 **domains** and an apparent transmembrane **domain** near the N terminus. The name tricalbins is suggested for these proteins, corresponding to the open reading frames YOR086c (TCB1), YNL087w (TCB2), and YML072c (TCB3). An antiserum was raised against the C-terminal portion of tricalbin 2 and used on Western blots to demonstrate that the corresponding protein is expressed in yeast and appears as a high-molecular-weight band at 130 kDa with smaller **fragments** at 39 kDa and 46 kDa. A **fusion protein** consisting of full length tricalbin 2 fused to the green **fluorescent protein** was expressed in cells and found to traffic from the cell surface to intracellular vesicles near the vacuole. A two-hybrid **interaction** screen with the C-terminal portion of tricalbin 2 indicated that tricalbin 2 **binds** the C-terminal portions of tricalbins 1 and 3 suggesting that

the tricalbins may form heterodimers in vivo. Tricalbin 2 also interacted with the activation **domain** of the pleiotropic drug resistance transcription factor Pdr1p. Combinatorial disruptions of the tricalbin genes revealed that tcb2 single mutants or tcb1, tcb3 double mutants have an altered vacuole morphology and are hypersensitive to cycloheximide. A screen for single-copy suppressors of the cycloheximide sensitivity of tricalbin mutants yielded RSP5, which encodes a C2-**domain**-containing, ubiquitin-conjugating ligase essential for receptor-mediated and fluid phase endocytosis. The results suggest that the tricalbins function as multimers in membrane-trafficking events and may provide insights into the roles of multi-C2-**domain** proteins, such as the synaptotagmins, in other organisms.

L8 ANSWER 6 OF 78 MEDLINE on STN
Full Text
AN 2004136672 MEDLINE
DN PubMed ID: 14985083
TI Anterograde and retrograde intracellular trafficking of fluorescent cellular prion protein.
AU Hachiya Naomi S; Watanabe Kota; Yamada Makiko; Sakasegawa Yuji; Kaneko Kiyotoshi
CS Department of Cortical Function Disorders, National Institute of Neuroscience, National Center of Neurology and Psychiatry, and Core Research for Evolutional Science and Technology, Japan Science and Technology Agency, Tokyo 187-8502, Japan.
SO Biochemical and biophysical research communications, (2004 Mar 19) 315 (4) 802-7.
Journal code: 0372516. ISSN: 0006-291X.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200404
ED Entered STN: 20040320
Last Updated on STN: 20040421
Entered Medline: 20040420
AB In order to investigate the microtubule-associated intracellular trafficking of the NH2-terminal cellular prion protein (PrPC) **fragment** [Biochem. Biophys. Res. Commun. 313 (2004) 818], we performed a real-time imaging of fluorescent PrPC (**GFP**-PrPC) in living cells. Such **GFP**-PrPC exhibited an anterograde movement towards the direction of plasma membranes at a speed of 140-180 nm/s, and a retrograde movement inwardly at a speed of 1.0-1.2 microm/s. The anterograde and retrograde movements of **GFP**-PrPC were blocked by a kinesin family inhibitor (AMP-PNP) and a dynein family inhibitor (vanadate), respectively. Furthermore, anti-kinesin antibody (alpha-kinesin) blocked its anterograde motility, whereas anti-dynein antibody (alpha-dynein) blocked its retrograde motility. These data suggested the kinesin family-driven anterograde and the dynein-driven retrograde movements of **GFP**-PrPC. Mapping of the interacting **domains** of PrPC identified amino acid residues indispensable for **interactions** with kinesin family: NH2-terminal mouse (Mo) residues 53-91 and dynein: NH2-terminal Mo residues 23-33, respectively. Our findings argue that the discrete N-terminal amino acid residues are indispensable for the anterograde and retrograde intracellular movements of PrPC.

L8 ANSWER 7 OF 78 MEDLINE on STN
Full Text
AN 2004353620 MEDLINE
DN PubMed ID: 15255944

TI Insulin receptor substrate of 53 kDa links postsynaptic shank to PSD-95.
AU Soltau Michaela; Berhorster Kerstin; Kindler Stefan; Buck Fritz; Richter Dietmar; Kreienkamp Hans-Jurgen
CS Institut fur Zellbiochemie und klinische Neurobiologie, Universitatsklinikum Hamburg-Eppendorf, Hamburg, Germany.
SO Journal of neurochemistry, (2004 Aug) 90 (3) 659-65.
Journal code: 2985190R. ISSN: 0022-3042.
CY England: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200409
ED Entered STN: 20040717
Last Updated on STN: 20040911
Entered Medline: 20040910
AB The insulin receptor substrate of 53 kDa (IRSp53) is a target of the small GTPase cdc42 which is strongly enriched in the postsynaptic density of excitatory synapses. IRSp53 interacts with the postsynaptic shank1 scaffolding molecule in a cdc42 regulated manner. The functional significance of the cdc42/IRSp53 pathway in postsynaptic sites is however, unclear. Here we identify PSD-95 as a second synaptic **interaction** partner of IRSp53. **Interaction** is mediated by a C-terminal PDZ binding motif in IRSp53 and the second PDZ **domain** of PSD-95. In HEK cells, overexpressed IRSp53 induces filopodia and targets PSD-95 into these processes. Immunoprecipitation and immunocytochemistry experiments demonstrate that the **interaction** occurs at postsynaptic sites in the brain. By virtue of its PDZ-binding and SH3 **domains**, IRSp53 is capable of inducing the formation of a triple complex (shank1/IRSp53/PSD-95).

L8 ANSWER 8 OF 78 MEDLINE on STN
Full Text
AN 2004029767 MEDLINE
DN PubMed ID: 14709720
TI A role for the spectrin superfamily member Syne-1 and kinesin II in cytokinesis.
AU Fan Jun; Beck Kenneth A
CS Department of Cell Biology and Human Anatomy, School of Medicine, University of California, Davis, CA 95616, USA.
NC GM59353-02 (NIGMS)
SO Journal of cell science, (2004 Feb 1) 117 (Pt 4) 619-29.
Journal code: 0052457. ISSN: 0021-9533.
CY England: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200409
ED Entered STN: 20040121
Last Updated on STN: 20040930
Entered Medline: 20040929
AB Expression of a dominant negative **fragment** of the spectrin family member Syne-1 causes an accumulation of binucleate cells, suggesting a role for this protein in cytokinesis. An association of this **fragment** with the C-terminal tail **domain** of the kinesin II subunit KIF3B was identified by yeast two-hybrid and co-precipitation assays, suggesting that the role of Syne-1 in cytokinesis involves an **interaction** with kinesin II. In support of this we found that (1) expression of KIF3B tail **domain** also gives rise to multinucleate cells, (2) both Syne-1 and KIF3B localize to the central spindle and midbody during cytokinesis in a detergent resistant and ATP sensitive manner and (3) Syne-1 localization is blocked by expression of KIF3B tail. Also, membrane vesicles containing syntaxin

associate with the spindle midbody with identical properties. We conclude that Syne-1 and KIF3B function together in cytokinesis by facilitating the accumulation of membrane vesicles at the spindle midbody.

L8 ANSWER 9 OF 78 MEDLINE on STN
Full Text
AN 2004392329 MEDLINE
DN PubMed ID: 15296087
TI New chimera proteins for fluorescence correlation spectroscopy.
AU Olah Z; Trier U; Sauer B; Schafer-Korting M; Kleuser B
CS National Institute of Dental and Craniofacial Research, Pain and Neurosensory Mechanisms Branch, National Institutes of Health, Bethesda, USA.
SO Die Pharmazie, (2004 Jul) 59 (7) 516-23.
Journal code: 9800766. ISSN: 0031-7144.
CY Germany: Germany, Federal Republic of
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200409
ED Entered STN: 20040807
Last Updated on STN: 20040904
Entered Medline: 20040903
AB A new class of chimera proteins has been developed. They are ideally suited for detection by fluorescence correlation spectroscopy (FCS), a new technology to analyze molecular **interactions**. The molecular structure of these chimera proteins consists of four **domains**: a N-terminal (His)6-tag for affinity chromatography followed by an eight amino acid epitope for immunodetection, a polypeptide affinity **domain** (ADF) for target specific **interaction** and a C-terminal Green **Fluorescent Protein** (GFPuv) for reporting of **interaction** with the target by FCS. We designed, prepared and characterized a prototype of ADF-**GFP** proteins capable of specific **interaction** with DNA **fragments** bearing nuclear factor (NF)-kappaB sites. ADF NF-kappaB p50 and a non-DNA-binding deletion mutant (p35) combined with GFPuv were inserted in a procaryotic vector and expressed in E. coli. Following affinity purification the fluoroproteins p50-GFPuv and p35-GFPuv were employed in specific protein-protein and protein-DNA **interaction** studies. FCS analysis as well as EMSA showed that p50-GFPuv revealed a fully functional ADF. We present a model for the preparation of **GFP fusion proteins** capable of specific **interaction** with proteins, lipids or nucleic acids. The rational design allows any polypeptide **fragment** to be incorporated into the chimeric protein. So a new series of bio-molecules with different binding specificities and assays can be developed.

L8 ANSWER 10 OF 78 MEDLINE on STN
Full Text
AN 2003612587 MEDLINE
DN PubMed ID: 14576163
TI Insulin-like growth factor-independent effects mediated by a C-terminal metal-binding **domain** of insulin-like growth factor binding protein-3.
AU Singh Baljit; Charkowicz Dona; Mascarenhas Desmond
CS Protigen, Inc, Sunnyvale, California 94085, USA.
SO Journal of biological chemistry, (2004 Jan 2) 279 (1) 477-87.
Journal code: 2985121R. ISSN: 0021-9258.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200403

ED Entered STN: 20031230
Last Updated on STN: 20040304
Entered Medline: 20040303

AB Insulin-like growth factors (IGFs) play a central role in the integration of proliferative and survival responses of most mammalian cell types. IGF-binding protein-3 (IGFBP-3) influences IGF action directly as a carrier of IGFs but also modulates these actions indirectly via independent mechanisms involving **interactions** with plasma, extracellular matrix and cell surface molecules, conditional proteolysis, cellular uptake, and nuclear transport. Here we demonstrate that a short C-terminal metal-binding **domain** (MBD) of IGFBP-3 mediates binding to metals. MBD epitopes, sequestered in the intact molecule, are unmasked by incubation in the presence of ferrous (but not ferric or zinc) ions. An isolated 14-mer MBD peptide triggered apoptotic effects in stressed HEK293 cells as effectively as IGFBP-3. The MBD, which encompasses a nuclear localization sequence and an adjacent putative caveolin-binding sequence, mobilizes rapid cellular uptake and nuclear localization of unrelated proteins such as green **fluorescent protein** and streptavidin-horseradish peroxidase conjugate. Metal ions stimulate MBD-mediated cellular/nuclear uptake in vivo. Cross-linking studies showed a direct physical **interaction** of MBD with integrins alphav and beta1, caveolin-1, and transferrin receptor. MBD-mediated protein mobilization and pro-apoptotic effects are inhibited by nystatin but not chlorpromazine, suggesting an involvement of caveolar-mediated endocytosis. However, MBD effects are inhibited by antibodies to transferrin receptor or integrins. These results are discussed with particular reference to the cell target specificity of IGFBP-3 in disease processes such as cancer and atherosclerosis.

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=> d his

     (FILE 'HOME' ENTERED AT 10:02:55 ON 15 OCT 2004)

     FILE 'MEDLINE, BIOSIS' ENTERED AT 10:03:06 ON 15 OCT 2004
L1            43 S PROTEIN FRAGMENT COMPLEMENTATION ASSAY
L2            13 S L1 AND (FLUORESCENT OR GFP)
L3             8 DUPLICATE REMOVE L2 (5 DUPLICATES REMOVED)
L4          1409 S (FLUORESCENT OR GFP) AND FUSION AND BIND
L5          1896 S (FLUORESCENT PROTEIN OR GFP) AND FUSION PROTEIN AND (BIND OR
L6           148 S L5 AND FRAGMENT
L7            91 S L6 AND DOMAIN
L8            78 DUPLICATE REMOVE L7 (13 DUPLICATES REMOVED)

=> s l8 and py<1998
L9             1 L8 AND PY<1998

=> d bib ab

L9   ANSWER 1 OF 1     MEDLINE on STN
Full Text
AN   97075105     MEDLINE
DN   PubMed ID: 8917531
TI   Expression in yeast of binding regions of karyopherins alpha and beta
     inhibits nuclear import and cell growth.
AU   Enenkel C; Schulke N; Blobel G
CS   Laboratory of Cell Biology, Rockefeller University, Howard Hughes Medical
     Institute, New York, NY 10021, USA.
SO   Proceedings of the National Academy of Sciences of the United States of
     America, (1996 Nov 12) 93 (23) 12986-91.
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Journal code: 7505876. ISSN: 0027-8424.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199612
ED Entered STN: 19970128
Last Updated on STN: 20000303
Entered Medline: 19961230

AB Using truncated forms of recombinant yeast karyopherins alpha and beta in in vitro binding assays, we mapped the regions of karyopherin alpha that **bind** to karyopherin beta and the regions of karyopherin beta that interact with karyopherin alpha and with Ran-GTP. Karyopherin alpha's binding region for karyopherin beta was localized to its N-terminal **domain**, which contains several clusters of basic residues, whereas karyopherin beta's binding region for karyopherin alpha was localized to an internal region containing two clusters of acidic residues. Karyopherin beta's binding region for Ran-GTP overlaps with that for karyopherin alpha and comprises at least one of the two acidic clusters required for karyopherin alpha binding in addition to further downstream determinants not required for karyopherin alpha binding. Overexpression in yeast of **fragments** containing either karyopherin beta's binding region for alpha and Ran-GTP or karyopherin alpha's binding region for beta resulted in sequestration of most of the cytosolic karyopherin alpha or karyopherin beta, respectively, in complexes containing the truncated proteins. As these binding region-containing **fragments** lack other **domains** required for function of the corresponding protein, the overexpression of either **fragment** also inhibited in vivo nuclear import of a model reporter protein as well as cell growth.

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